60.001

Multi-resistant Enterobacteriaceae

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Resistance to multiple antimicrobial agents is becoming more frequently seen amongst the Enterobacteriaceae world-wide. Much of this is result of the accumulation of resistances inside integrons. Thus, resistance to penicillins, beta-lactamase inhibitor combination, cephalosporins, monobactams, carbapenems, fluoroquinolones, aminoglycosides, tetracyclines and folate antagonists can be found in various linked combinations within the family. The most problematic species is *Klebsiella pneumoniae* (KPNE), with *Escherichia coli* (ECOL) and *Enterobacter* species (ENTR) showing rising rates of multi-resistance. The increasing rates of linked resistance have created significant problems because of limited treatment choices. Options for treatment of serious infections caused by extended-spectrum beta-lactamase-(ESBL)-producing KPNE and ECOL include carbapenems, considered the drugs of choice by many, and, only if susceptible, fluoroquinolones. Aminoglycosides have not been favoured as the patients with multi-resistant strains are the most vulnerable to the toxic effects. Trimethoprim-sulfamethoxazole, if tested as susceptible, may be used for minor infections, but there is little published experience with its use in serious infections. Tetracyclines are generally not favoured for infections caused by Enterobacteriaceae. Carbapenems are also favoured for treatment of serious infections caused by ENTR. Again aminoglycosides have been used but have their attendant problems, including failure to prevent the emergence of stably-derepressed mutants when used in combination with third-generation cephalosporins. The recent emergence of carbapenemases in Enterobacteriaceae in some parts of the world, especially KPC series enzymes in KPNE and metallo-enzymes in a number of species, have left few viable options for treatment. Most experience has been gained with polymyxins, especially colistin methanosulfonate. However, doubts about the efficacy of this class remain, related both pharmacodynamics, and to the potential for resistance selection. The only readily available alternative is tigecycline, but there is limited experience with this agent and uncertainty about the adequacy of the current dosing regimens. The lack of novel agents active against Gram-negatives in the development pipeline heralds a bleak future for treating multi-resistant Enterobacteriaceae.

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60.002

Carbapenem-resistant Pseudomonas and Acinetobacter

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Over the last decade infections caused by multi drug-resistant (MDR) gram-negative bacteria have become a gram-negative bacteria, particularly Klebsiella spp., E coli, P. aeruginosa, and Acinetobacter spp. have become increasingly difficult to treat due to the rising incidence of drug resistance and the limited number of antimicrobial agents that are effective against them.

Acquired carbapenemases are increasingly reported in Pseudomonas and Acinetobacter isolates world wide. The emergence of these carbapenem-resistant P aeruginosa and Acinetobacter species has provided a particularly difficult challenge for clinicians with most carbapenemase producers being broadly resistant to beta-lactams, and many are also resistant to fluoroquinolones and aminoglycosides. Due to the lack of therapeutic options in these patients who are often critically ill, clinicians are often faced with using older and more toxic antibiotics such as polymyxins and minocycline. Sulbactam which has inherent activity against A baumannii has also been found to be useful in the treatment of these infections. Polymyxins are now being commonly used to treat these multi drug resistant A baumanii and P aeruginosa with variable success. Additionally, combination antimicrobial therapy is frequently employed to treat infections caused by such multidrug-resistant strains adding to the potential toxicity and cost of treatment.

Clearly the ever growing threat of the rise MDR gram negative infections including carbapenem resistant P. aeruginosa and Acinetobacter spp cannot be answered by the development of new antimicrobial agents alone. A multipronged strategy that includes adherence to infection control principles and antimicrobial stewardship programs including rational use of current antimicrobial agents must remain the main stay of the response to this growing healthcare threat.

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Ceftriaxone-resistant Salmonella

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Salmonella resistant to extended-spectrum cephalosporins (e.g. ceftriaxone) has become a worldwide problem, with over 43 countries reporting cases. These infections have been associated with increased risk of bloodstream infections, longer duration of hospitalization and pose a treatment challenge, particularly in children. Common mechanisms of this antimicrobial resistance are mediated by extended-spectrum beta-lactamases and plasmid-mediated cephalosporinases, with the CMY-2 being the most widely disseminated enzyme. In humans, Salmonella enterica serotypes Typhimurium, Enteriditis and Newport are the most common serovars associated with ceftriaxone resistance. The use of antimicrobial agents in livestock, including cattle, has been associated with the emergence of antimicrobial-resistant nontyphoidal Salmonella strains and with the dissemination and transmission of these strains to humans. In this presentation, an overview of the epidemiology, risk factors, antimicrobial resistance mechanisms and